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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,629	03/09/2004	Youngro Byun	T9983.A	4749

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EXAMINER	
SELLMAN, CACHET I	
ART UNIT	PAPER NUMBER
1792	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,629	BYUN ET AL.	
	Examiner	Art Unit	
	CACHET I. SELLMAN	1792	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of the amendment filed by the applicant on 12/21/2007, in which claims 1, 5 and 6 were amended and claims 8-16 were added. Claims 1-16 are currently pending in U.S. Application Serial No. 10/797629.

Claim Rejections - 35 USC § 112

The 112, 2nd paragraph rejection of claim 5 in the previous office action is withdrawn due to applicant's amendment to the claim correcting the antecedent basis.

Response to Arguments

1. Applicant's arguments with respect to claims 1-7 have been considered but are moot in view of the new ground(s) of rejection. The applicant amended the independent claims to include the limitation of having a heparinized polymer having **a macromolecule, a hydrophobic material and heparin bound together with covalent bonds**.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Byun et al. (US 6245753).

3. Byun et al. discloses a composition comprising an heparinized polymer. The heparinized polymer comprises a macromolecule, a hydrophobic material and heparin bound by covalent bonds (see abstract, col. 2, lines 33-44, col. 4, line 66 - col. 5, line 2 and claim 11). the composition is applied to a medical device which comes in contact

with blood to prevent thrombosis (see abstract, col. 4, lines 22-23, col. 4, lines 62-66) as required by **claim 6**.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1-12, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al. (US 5879697) in view of Bernacca et al (US 6251142) and Byun et al. (US 6245753).

Ding et al. discloses a process for coating a medical device (i.e. stent) (see col. 4, lines 58-67) with an underlayer (reservoir layer) and a top layer. The coating allows for timed and prolonged pharamacological activity on the surface of the medical device (see abstract). The reservoir layer comprises a polymer and a biologically active material (see col. 5,lines 31-37). The reservoir layer is formed by combining the polymer and the active agent with a solvent and is then applied to the stent (see example 1).

The toplayer comprises an ionic surfactant drug complex which can also contain a polymer (see col. 8, lines 15-30). The drug used in the top layer is heparin (see examples).

Ding et al. fails to teach that the second layer comprises a macromolecule, a hydrophobic material and heparin bound together with covalent bonds, and cleaning the stent with a washing agent as required by **claim 1**.

However, it was well known in the art at the time the invention was made to clean a stent prior to coating in order to remove contaminants and to insure that the coatings will adhere to the stent such as taught by Bernacca et al (US 6251142) therefore one would have been motivated to wash the stent as taught by Bernacca et al. prior to coating in order to ensure sufficient adherence of the coating to the stent.

Byun et al. discloses a coating which can be used on medical devices in order to control the release of heparin from a stent. The process of Byun et al. uses a hydrophobic heparin derivative having high bioactivity for controlled release systems and for improving biocompatibility in medical devices. The composition comprises a polysaccharide covalently bonded to a hydrophobic agent where the polysaccharide is heparin or heparin sodium (see col. 2,lines 33-40). The hydrophobic agent can be bile acids, sterols, and alkanoic acids (see col. 2,lines 42-44). The hydrophobic agent and heparin are mixed and bonded with a polymeric carrier (see col. 4,line 66- col. 5, line 2). The polymeric carrier can be polyethylene oxide-polycaprolactone copolymers, polyurethane polymers, silicone, etheylene vinyl acetate polymers, hydrogels, collagen, gelatin or mixtures thereof (see claim 11).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the process of Ding et al. to include the top coating comprising the composition of Byun et al. One would have been motivated to do so because both are directed towards controlled rate release in medical devices especially stents which comprise heparin. Furthermore, Byun et al. teaches that such a coating improves biocompatibility and high bioactivity.

The underlayer can comprise of more than one drug/ bioactive agent (see col. 7, lines 60-65) as required by **claim 2**. The polymer and agent mixture can be applied by dipping the stent into the mixture or spraying (see col. 7, lines 29-31) as required by **claims 3 and 4**.

As started above, Ding et al. modified by Byun et al. teach the use of the top coating which is used to prevent burst release by adding the rate controlling layer as required by **claim 5**.

As stated above the composition applied to the medical device is an antithrombogenic coating as required by **claim 6**.

The polymer film can be formed of polyolefins, polyurethanes, silicones, polyesters, polycapralactones (see col. 5, lines 37-64) as required by **claim 8**. The biologically active agent can be antithrombotic, anticoagulants, antiplatlet, antiinflammatory, antibiotics, etc. (see col. 6, lines 23-40) as required by **claim 9**. The first layer can comprise a second active agent as required by **claim 10**. The macromolecule can be collagen, gelatin, polyurethanes (see claim 11 of Byun) as required by **claims 12 and**

14. The hydrophobic material is bile acids, sterols, and alkanoic acids as required by **claim 15**. The heparin can be heparin derivative as required by **claim 16**.

7. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al. in view of Bernacca et al. (US 6251142) and Byun et al. (US 7129224).

Ding et al. discloses a process for coating a medical device (i.e. stent) (see col. 4, lines 58-67) with an underlayer (reservoir layer) and a top layer. The coating allows for timed and prolonged pharamacological activity on the surface of the medical device (see abstract). The reservoir layer comprises a polymer and a biologically active material (see col. 5,lines 31-37). The reservoir layer is formed by combining the polymer and the active agent with a solvent and is then applied to the stent (see example 1). The toplayer comprises an ionic surfactant drug complex which can also contain a polymer (see col. 8, lines 15-30). The drug used in the top layer is heparin (see examples).

Ding et al. fails to teach that the second layer comprises a macromolecule, a hydrophobic material and heparin bound together with covalent bonds, and cleaning the stent with a washing agent as required by **claim 1**.

However, it was well known in the art at the time the invention was made to clean a stent prior to coating in order to remove contaminants and to insure that the coatings will adhere to the stent such as taught by Bernacca et al (US 6251142) therefore one would have been motivated to wash the stent as taught by Bernacca et al. prior to coating in order to ensure sufficient adherence of the coating to the stent.

Byun et al. ('224) teaches a hydrophobic heparin conjugates that are prepared by convalently binding a polymer to heparin and a hydrophobic agent. The conjugate has good antithromobenic effects due to hydrophobicity and can be effectively used in coating medical device surfaces (abstract).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the process of Ding et al. to include the top coating comprising the composition of Byun et al. One would have been motivated to do so because both are directed towards controlled rate release in medical devices especially stents which comprise heparin. Furthermore, Byun et al. teaches that such a coating improves biocompatibility and high bioactivity.

The underlayer can comprise of more than one drug/ bioactive agent (see col. 7, lines 60-65) as required by **claim 2**. The polymer and agent mixture can be applied by dipping the stent into the mixture or spraying (see col. 7, lines 29-31) as required by **claims 3 and 4**.

As started above, Ding et al. modified by Byun et al. teach the use of the top coating which is used to prevent burst release by adding the rate controlling layer as required by **claim 5**.

As stated above the composition applied to the medical device is an antithrombogenic coating as required by **claim 6**.

The polymer film can be formed of polyolefins, polyurethanes, silicones, polyesters, polycapralactones (see col. 5, lines 37-64) as required by **claim 8**. The biologically active agent can be antithrombotic, anticoagulants, antiplatlet, antiinflammatory,

antibiotics, etc. (see col. 6, lines 23-40) as required by **claim 9**. The first layer can comprise a second active agent as required by **claim 10.**

The macromolecule can be a synthetic macromolecule such as polydiences, polyalkenes, polyacetylenes, polyacrylic acid, and derivatives, polyvinyl ethers, polyvinyl alcohols, poly vinyl halides, polystyrene, polyoxides etc. (see col. 3,lines 53-63); a protein such as protamine, polylysine, polyaspartic acid, polyglutamic acid (see col. 3,lines 63-64); or a biopolymer such as polysaccharides, gelatin, collagen, alginate, hyaluronic acid, alginic acid etc. (see col. 3,l ines 65-67) as required by **claims 11-14**. The hydrophobic mateiral can be octadeclyamine, alkonoic amine, bile acids, sterols, or alkanoic acis (see col. 5,lines 34-40) as required by **claim 15**.

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Tsang et al. (US 5955588) teaches an anti-thrombogenic coating composition used for blood contacting devices having a covalent complex of hydrophobic silyl moieties directly bonded to a heparin molecule via covalent bonding. Delden et al. ("The effect of protein absorption on the anticoagulant activity of surface immobilization heparin") teaches heparin-albumin-polystyrene bead conjugates that are formed using covalent linkages through amide bonds (see page 729). Zamora et al. (US 6596699) teaches a coating material formed of a macromolecule, hydrophobic material and heparin where the hydrophobic material and heparin are bonded with covalent bonds and the heparin and macromolecule are bonded through non covalent bonds.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CACHET I. SELLMAN whose telephone number is (571)272-0691. The examiner can normally be reached on Monday through Friday, 7:00 - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Timothy Meeks can be reached on 571-272-1423. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner
Art Unit 1792

/C. I. S./
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/William Phillip Fletcher III/
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